milder, such as tolerable thirst, urinary, vascular, ocular or skin manifestations, the patient will need a diet and a trial of oral antidiabetic drugs. If these fail, insulin may be needed sooner or later. If the patient has a known diabetic relative or shows signs of renal or vascular disease or cataract, I think the blood sugar should be controlled to avoid further tissue changes and ischæmia. Obese patients usually respond well to diet, but oral antidiabetic drugs should be used if necessary to secure 'normoglycæmia' in them and in some of the leaner patients. The remainder with two-hour blood sugar over 120 mg/100 ml should be given advice about health, diet and exercise and kept under surveillance every year or two. A bout of over-eating or under-exercising may overtax their endogenous insulin resources and seriously aggravate their hyperglycæmia.

REFERENCES
Wilkerson H L C & Krall L P
(1947) *J. Amer. med. Ass.* **135**, 209
(1953) *J. Amer. med. Ass.* **152**, 1322

Dr Harry Keen
(Guy's Hospital Medical School, London)

The Bedford Survey: A Critique of Methods and Findings

The Bedford Survey provided an opportunity for a critical study of screening methods for identifying undiagnosed diabetics; it also furnished a picture of glucose tolerance in the population at large, and created new problems and ideas, some of which will be dealt with in this paper.

If the aim of the Survey was to identify as suspected diabetics all those people in Bedford whose capillary blood sugar two hours after 50 grams glucose by mouth (two-hour B.S.) would have been 120 mg/100 ml or more, then it failed quite remarkably. Accepting the random sample findings as representative of the population at large, one would have expected to find about 15% of the co-operating population, some 3,900 individuals in this two-hour B.S. class. In fact only 282, 1% of the population, were identified. This huge discrepancy points to inadequacy in the preliminary screening procedure, the 'post-prandial' urine test for sugar. The data of Kenny & Chute (1953) demonstrated the surprisingly small blood sugar rise after breakfast and lunch in a population group. The fact that about two-thirds of the Bedford Survey glycosurics were found to have two-hour B.S. levels below 120 mg/100 ml at glucose tolerance test (G.T.T.) suggests that the 'challenge' of the meal evoked glycosuria less successfully in those with chronic hyperglycæmia than in those with low renal thresholds or transient hyperglycæmic peaks.

The relationship of glycosuria to the two-hour B.S. is further explored in Table 1 which shows the frequency distribution of two-hour B.S. levels in the 295 members of the random sample whose urines were retested between the sixty-minute period and the ninety-minute period when they came for G.T.T. The Table also shows the two-hour B.S. levels of the 12 survey glycosurics drawn by chance in this sample, and those of the 90 whose urines were positive when retested at G.T.T. It can be seen that a 4% incidence of glycosuria under survey conditions rose to 30% after the 50 gram glucose load at G.T.T. Many more of the people with the higher two-hour B.S. values were glycosuric at G.T.T. than at the survey; of the 50 with two-hour B.S. values of 120 mg/100 ml or more, only 10% were glycosuric at survey while 54% became glycosuric at G.T.T.; of the 10 with levels of 160 mg/100 ml or more, 9 became positive at G.T.T. The glucose load also provoked glycosuria in a large number of people with two-hour B.S. levels below 120 mg/100 ml (3% at survey against 26% at G.T.T.), but analysis of the glucose tolerance curves of these glycosurics showed that 57% of them achieved blood sugar levels of 180 mg/100 ml or more at some stage of the G.T.T. compared with only 16% of non-glycosurics.

Table 1
Two-hour blood sugar and glycosuria in 295 members of random sample

Two-hour blood sugar (mg/100 ml)	*No. of persons in group*	*Positive urine test*	
		At survey	*At G.T.T.*
40–59	5	0	3
60–79	81	2	22
80–99	90	3	23
100–119	69	2	15
40–119	245	7 (3%)	63 (26%)
120–139	31	1	15
140–159	9	0	3
160–179	5	2	5
180–	5	2	4
Over 120	50	5 (10%)	27 (54%)
Total	295	12 (4%)	90 (30%)

The distribution of raised two-hour B.S. levels among G.T.T. glycosurics and non-glycosurics by age and sex, is examined in Fig 1. This shows that a larger proportion of women than of men had a two-hour B.S. of 120 mg/100 ml or more; with increasing age, more glycosurics had raised two-hour B.S. levels (and so, to a lesser extent, did non-glycosurics). Among older people, more

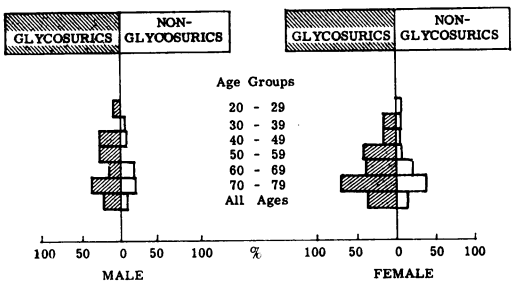

Fig 1 *Elevated two-hour blood sugars in G.T.T. glycosurics and non-glycosurics. Horizontal bars denote percentage with two-hour B.S. of 120 mg/100 ml or more*

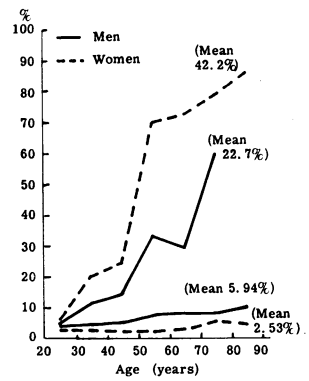

Fig 2 *Incidence of glycosuria at survey and of raised two-hour B.S. in glycosurics, by age and sex. Lower two lines show percentage of population with glycosuria. Upper two lines show percentage of glycosurics with two-hour B.S. of 120 mg/100 ml and over*

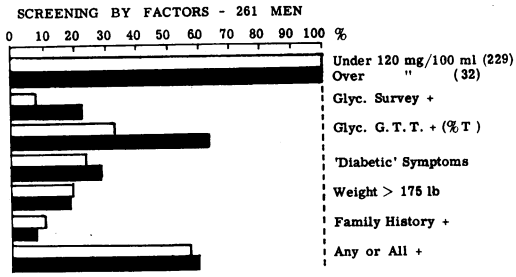

Fig 3A

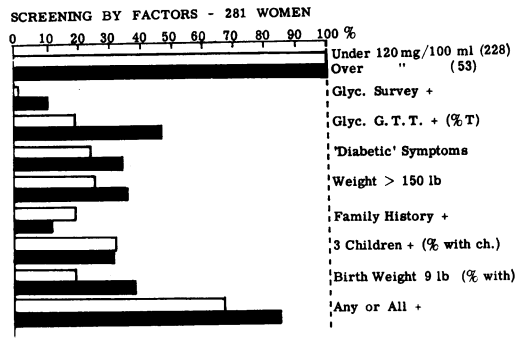

Fig 3B

Fig 3A, B *Differentiating value of various factors between people with higher and lower two-hour B.S. levels. Black columns represent incidence of factor shown on right among those with two-hour B.S. of 120 mg/100 ml or more, and white columns among those with two-hour B.S. less than 120 mg/100 ml. Rates calculated from random sample data*
Glyc. Survey+ = glycosuric at main survey
Glyc. G.T.T.+(%T)= glycosuric at G.T.T. as % of the 295 retested
'Diabetic' Symptoms=thirst, polyuria, recent visual change, skin sepsis
Family History+ = positive family history of diabetes mellitus. 3 Children + (% with ch.) = women with 3 live births or more, as % of all women with children
Birth Weight 9 lb + (% with) = women with baby of 9 lb or more at birth, as % of all women with babies

women than men had raised two-hour B.S. levels in the absence of glycosuria. The figure suggests that the chance that glycosuria represents a raised blood sugar level increases with age, and is higher in women than in men. Support for this conclusion is to be found in a similar analysis of the two-hour B.S. levels of all those people found to be glycosuric in the survey (Fig 2). The lower pair of lines show that the incidence of glycosuria was higher in men than women and rose a little with age. By contrast, the proportion of these survey glycosurics with two-hour B.S. values of 120 mg/100 ml or more (upper pair of lines) rose rapidly with age and was higher in women than in men. There are two explanations for these results. The first, and the less likely, is that non-diabetic glycosuria in youth presages diabetes in later life which develops more rapidly in women than in men. A more reasonable explanation is that the renal threshold for glucose rises with age, and that at all ages it is higher in women than men. Thus, as age advances, increasingly high levels of blood sugar are required to produce glycosuria; at any age, the level requires to be higher in women than in men. These relationships have importance in judging the significance of a positive urine test, for, while glycosuria in a young man carries only a 5% chance of representing the higher two-hour B.S. levels, in older women the chance is about 80%.

These limitations of urine testing led us to examine other factors which might have differentiated between people with higher and lower two-hour B.S. levels. Figs 3A and 3B show graphically, for men and women respectively, the differentiating value of a number of these factors taken from the random sample data. For

comparison, the efficiency of the urine test is also expressed in the same way. The length of the black bar represents the proportion of people with two-hour B.S. levels of 120 mg/100 ml or more who screened positive to the particular factor; ideally it should be 100%. The degree to which it falls short of this value represents the false negatives. The proportion of false positives is shown by the length of the white bar which, ideally, should be 0%. In men, none of the factors examined had discriminating value, and among the women only the history of bearing a baby with a birth weight of 9 lb or more pointed strongly to a high two-hour B.S. It remains to be seen whether different 'settings' of the dividing blood sugar level, or values of the screening factors would yield more useful discrimination. To identify the group with two-hour B.S. of 120 mg/100 ml and over, we conclude that there is little alternative to direct measurement of the blood sugar; for this, a simple blood sugar screening device, perhaps along the lines of the Clinistix, would be invaluable.

It must be emphasized that our choice of a two-hour B.S. of 120 mg/100 ml as a dividing level was quite arbitrary. Among people in the random sample there was no obvious two-hour B.S. level which recommended itself instead. While the apparently continuous distribution of two-hour B.S. values across the range regarded as demarcating normal from abnormal in this general population sample raises fascinating speculations about the nature of diabetes and its ætiology, the critical question for the clinician is: 'Who needs treatment?' An operational diagnosis has to be made on the basis of the blood sugar results. Harting & Glenn (1951) left '. . . the decision concerning the degree of hyperglycæmia and glycosuria necessary for a definite diagnosis of diabetes . . . to the judgment of the person's physician'. We argued along the following lines: All clinicians would accept a two-hour B.S. of 200 mg/100 ml or more as falling into the diagnostic category 'diabetes mellitus', so we sent people with these levels to their family doctors with a definite diagnosis and a recommendation that they should be referred to the local diabetic clinic. A two-hour B.S. of less than 120 mg/100 ml would be accepted as excluding the diagnosis and we told people in this class that they were normal at present.

People with intermediate values (two-hour B.S. 120 – 199 mg/100 ml) were interviewed in small groups and their 'borderline' status explained to them. With their agreement, we started for them a special 'borderline clinic' in Bedford, where they have been seen and examined at six-monthly intervals since the survey ended. They have been allocated at random to one of a number of treatment groups, and at each clinic visit special attention is being paid to the eyes, kidneys, peripheral nerves and blood vessels, along with repeated measurements of two-hour B.S., and other biochemical factors. Similar observations have been made on a matched control group composed of members of the random sample who were proved 'normal' in respect of the blood sugar at G.T.T.

We hope that our study of the 'borderline' group will, in time, answer the following questions: (1) In what ways, if any, do 'borderline' diabetics differ from normals? (2) Is there a critical level of blood sugar at which 'diabetic damage' starts? (3) If so, will treatment postpone or prevent the damage?

Conclusions

The Bedford Survey has emphasized the insensitivity of urine testing as a preliminary screening procedure in the identification of undiagnosed diabetics. Sensitivity may be greatly improved by testing the urine after a standard 50 g glucose load, but this has the disadvantage of yielding many false positive results. Most of these are among younger people, particularly men, and this probably reflects the fact that the renal threshold for glucose is lower in men than women and that it rises with age. As a screening procedure, blood sugar measurement after a glucose load is the method of choice.

Findings in the random sample of the population suggest that there is a large number of people with marginal elevation of blood sugar levels who are not readily assignable to either diabetic or normal categories. Careful evaluation of such people by means of controlled trials of treatment are of high importance, for not only may they be candidates for the development of symptomatic diabetes but it also seems possible to us that the widespread distribution of arterial disease and cataract in the population at large may in part be related to an unrecognized 'borderline' diabetic state.

REFERENCES

Harting D & Glenn B (1951) *New Engl. J. Med.* **245**, 48

Kenny A J & Chute A L (1953) *Diabetes. N.Y.* **2**, 187

Meeting February 15 1963

Professor D D Reid (*London*) read a paper entitled **International Comparison in Epidemiology.**